- (b) without contacting the surface with a vesicle, aligning the vesicles at a first set of locations adjacent to the surface of the substrate;
- (c) using mechanical pressure, controlling each of the chambers to eject a nanoliter volume of the fluid from each vesicle onto the surface of the substrate aligned with the vesicles, whereby an array of the fluid is deposited on the surface of the substrate.—
  - -41. A method of claim 40, further comprising the steps of:
- (d) moving the assembly of step (a) to align the vesicles at a second set of locations adjacent to the surface of the substrate;
  - (e) repeating steh (c); and
- (f) optionally repeating steps (d) and (e) to dispense fluid at additional sets of locations on the surface of the substrate.—
- —42. A method of claim 40, wherein the substrate has wells formed on the surface of the substrate for defining locations for receiving the fluid ejected from the vesicles.—
- —43. A method of claim 40, wherein the fluid comprises a solvent and a matrix material.—
- —44. A method of claim 43, including the further step of waiting a predetermined period of time to allow the solvent comprising the matrix material to evaporate from the fluid ejected onto the surface of the substrate leaving the matrix material deposited on the surface.—
- —45. A method of claim 44, further comprising repeating steps of (a) through (c) are repeated at the same locations on which the matrix material is deposited, wherein the chambers of the vesicles in the assembly contain a solvent comprising an analyte material, which upon ejection on the array of matrix material dissolves into the matrix.—
- —46. A method of claim 44, wherein steps of (a) through (f) are repeated at the same locations on which the matrix material is deposited, wherein the chambers of the vesicles in the assembly contain a solvent



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comprising an analyte material, which upon ejection on the array of matrix material dissolves into the matrix.—

- ---47. A method of claim 40, wherein the fluid comprises an analyte in a solvent.--
- —48. A method of claim 47, including the further step of waiting a predetermined period of time to allow the solvent comprising analyte to evaporate from the fluid ejected onto the surface of the substrate leaving the analyte material deposited on the surface.—
- —49. A method of claim 48, further comprising repeating steps of (a) through (c) are repeated at the same locations at which analyte is deposited, wherein the chambers of the vesicles in the assembly contain a solvent comprising a matrix material, which upon ejection onto the array of analyte dissolves into the analyte.—
  - —50. A method of claim 41, wherein:

the fluid comprises an analyte in a solvent;

the method includes the further step of waiting a predetermined period of time to allow the solvent comprising analyte to evaporate from the fluid ejected onto the surface of the substrate leaving the analyte material deposited on the surface; and

steps of (a) through (f) are repeated at the same locations at which analyte is deposited, wherein the chambers of the vesicles in the assembly contain a solvent comprising a matrix material, which upon ejection onto the array of analyte dissolves into the analyte.—

- —51. A method of claim 40, wherein the fluid comprises a mixture of analyte material and matrix material.—
- —52. A method of claim 40, including the further step of providing the resulting substrate with the array of material deposited thereon to a diagnostic tool for determining information representative of the composition of the deposited material.



—53. A method of claim 52, wherein the diagnostic tool comprises a mass spectrometer.

- —54. A method of claim 41, wherein the step of moving the assembly includes the step of rastering the assembly across the surface of the substrate.—
- —55. A method of claim 4, wherein the step of moving the assembly includes the step of determining an offset signal representative of a distance for moving the assembly to align the vesicles at a location adjacent to the first plurality of locations.—
- —56. A method of claim 40, including the further step of drawing a wash fluid into the chambers to rinse the chambers.—
  - —57. A method of claim 40, wherein:

each vesicle comprises a pin having a chamber of sufficiently narrow bore to allow the chamber to at least partially fill with fluid by capillary action; and

the vesicles of the assembly are contacted with a source of fluid to at least partially fill the chambers with a volume of fluid by capillary action.—

—58. A method of claim 57, wherein:

the chambers of the vesicles are connected to a pressure source; and a positive pressure from the pressure source is applied to the chamber to partially offset a volume of fluid that fills the chamber by capillary action.—

—59. A method of claim 40, wherein:

the chambers of the vesicles are connected to a pressure source that applies a negative pressure to the chamber; and

fluid is introduced into the vesicles by contact with a fluid source to at least partially fill the chambers with a volume of fluid by negative pressure.—

—60. A method of claim 40, wherein the substrate comprises material selected from the group consisting of silica, glass, dellulose, silicon, metal, plastic, polymer and metal-grafted polymer.—

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—61. A method of claim 40, wherein the substrate comprises a flat surface, a flat surface with pits, a solid or porous bead, a membrane or a pin.—

- —62. A method of claim, wherein the surface of the substrate is functionalized chemically, functionalized with beads or functionalized with dendrites of captured material.—
- —63. A method of claim 40, wherein the fluid comprises an oligonucleotide.—
  - -64. A method of claim 40, wherein:

the chambers of the vesicles are connected to a pressure source; and controlling the vesicles to eject fluid is effected by applying positive pressure to the chambers of the vesicles by the pressure source.—

—65. A method of claim 64, wherein the pressure in the chamber of the vesicle is sufficient to result in ejection of a spray of the fluid from the vesicle.—

—66. A method of claim 64, wherein the pressure in the chamber of the vesicle is selected to result in ejection of droplets of the fluid from the vesicle.—

- —67. A method of claim 40, wherein each vesicle of the assembly comprises an assembly having a capillary element for directing the fluid to the surface of the substrate and a transducer element for applying pressure to the jet to dispense the fluid.—
- —68. A method of claim 67, wherein the transducer element is disposed around the capillary and can transform an electrical pulse into mechanical deformation of the capillary, resulting in ejection of fluid from the capillary.—
- —69. A method of claim 67, wherein the transducer element is selected from the group consisting of piezoelectric, electric, electrorestrictive, magnetorestrictive and electromechanical transducers.—
- —70. A method for dispensing nanoliter volumes of a material as an array on the surface of a substrate, comprising the steps of:
- (a) providing a pin assembly having a plurality of elongated vesicles arranged as an array for dispensing a liquid therefrom, wherein each vesicle

comprises a solid shaft of material having an end for retaining a nanoliter volume of fluid:

- (b) loading a nanoliter volume of fluid comprising a liquid material from a fluid source onto the end of the vesicles of the pin assembly;
- (c) without contacting the surface with the vesicle, disposing the pin assembly to align the vesicles at a first set of locations adjacent to the surface of the substrate;
- (d) contacting the loaded fluid to the surface of the substrate aligned with the vesicles, whereby an array of material on the surface of a substrate is formed.—
  - -71. A method of claim 70, further comprising the steps of:
  - (e) repeating step (b);
- (f) moving the pin assembly to align the vesicles at a second set of locations adjacent to the surface of the substrate and adjacent to the first set of locations;
  - (g) repeating step (d); and
- (h) optionally repeating steps (e) through (g) to dispense material at additional locations on the substrate.—
- —72. A method of claim 70, wherein the substrate has wells formed on the surface of the substrate for defining locations for receiving the fluid ejected from the vesicle.—
- —73. A method of claim 70, wherein the solvent comprises a matrix material for mass spectroscopy.—
- —74. A method of claim 73, including the further step of waiting a predetermined period of time to allow the solvent comprising the matrix material to evaporate, whereby the matrix material is deposited on the surface.—
  - -75. A method of dain 74, wherein:

steps of (a) through (d) are repeated with the vesicles containing a solvent comprising an analyte material; and

the fluid of analyte material at the end of the vesicles is contacted with the evaporated matrix material on the surface of the substrate to dissolve the matrix material with the analyte material and thereby deposit a mixture of matrix and analyte material.—

- —76. A method of claim 70, wherein the material of the solvent comprises an analyte material.—
- —77. A method of claim 76, including the further step of waiting a predetermined period of time to allow the solvent comprising the analyte material to evaporate, whereby the analyte material deposited on the surface.—
  - -78. A method of claim 77, wherein:

steps of (a) through (d) are repeated with the vesicles containing a solvent complising a matrix material; and

the fluid of matrix material at the end of the vesicles is contacted with the evaporated analyte material on the surface of the substrate to dissolve the matrix material with the analyte material and thereby deposit a mixture of matrix and analyte material.—

—79. A method of claim 70, wherein the material of the solvent comprises a mixture of analyte material and matrix material.—

-80. Almethod of claim 70, including the further step of:

providing the substrate with the array of material disposed thereon to a diagnostic tool for determining information representative of the composition of the material.—

- —81. A method of claim 80, wherein the diagnostic tool comprises a mass spectrometer.—
- —82. A method of claim 71, wherein the step of moving the pin assembly includes the step of rastering the pin assembly across the surface of the substrate.—
- —83. A method of claim 71, wherein the step of moving the pin assembly includes the step of determining an offset signal representative of a

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distance for moving the pin assembly to align the vesicles at a location adjacent the first plurality of locations.—

- —84. A method of claim 70, wherein the substrate comprises material selected from the group consisting of silica, glass, cellulose, silicon, metal, plastic, polymer, and metal-grafted polymer.—
- —85. A method of claim 70, wherein the substrate comprises a flat surface, a flat surface with pits, a solid or porous bead, a membrane or a pin.—
- —86. A method of claim 70, wherein the surface of the substrate is functionalized chemically, functionalized with beads or functionalized with dendrites of captured material.—
- -87. The method of claim 1, wherein the vesicle is part assembly of vesicle elements, wherein each of vesicle comprises an interior chamber holding nanoliter volumes of fluid.—
  - -88. The method of claim 87, wherein:

the vesicles are inside a housing that has an interior chamber connected to a pressure source that will control the pressure within the interior housing; and

the pressure source provides pressure to chamber of the housing to regulate the flow of fluid through the interior chamber of each vesicle, thereby dispensing of defined nanoliter volumes of fluid from the vesicles.—

-89. The method of claim 1, wherein:

the vesicle has an interior chamber and forms part of an assembly comprising a plurality of vesicles and a transducer element mounted to each vesicle for driving fluid through the interior chamber to eject fluid by deforming the chamber; and

the transducer element deforms the chamber with sufficient pressure to spray the fluid from the pin or to cause a drop of fluid to extend from the

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chamber so that fluid can be passed to the substrate by contacting the drop to the surface of the substrate.—

-90. The method of claim 1, that is automated.-

Please amend claims 1-39 as follows:

1. A method for forming an array of a sample material on a surface of a substrate comprising: [the steps of]

providing a vesicle [having] that has an interior chamber containing a fluid comprising a solvent containing the sample material[,];

without contacting the surface with the vesicle, disposing said vesicle adjacent to a first location on said surface of the substrate[,];

providing mechanical pressure to the interior of the [controlling said] vesicle to eject from said chamber a nanoliter volume of the fluid to dispense said fluid at said first location of said surface of the substrate[,]; and

moving said vesicle to <u>each of</u> a set of positions adjacent [said] <u>to the</u> surface of the substrate, whereby <u>a nanoliter volume of</u> fluid is dispensed at each location of said set [for] forming [said] <u>an</u> array of sample material <u>on the substrate</u>.

- 2. (Amended) A method [according to] of claim 1, [including the further step of providing a], wherein the substrate [having] has wells formed [on said surface of the substrate] thereon for defining locations for receiving said fluid ejected from said chamber.
- 3. (Amended) A method [according to] of claim 1, [including the further steps of depositing] wherein the sample material comprises a matrix material for mass spectroscopy [on a surface of said substrate].
- 4. (Amended) A method [according to] of claim 3, including the further step of waiting a predetermined period of time to allow the solvent [of said] containing the matrix material to evaporate on the surface of the substrate thereby depositing the matrix material on the surface.



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- 5. (Amended) A method [according to] of claim 4, [wherein] further comprising [said step of] ejecting a nanoliter volume of fluid [includes the step of ejecting said fluid] containing an analyte material onto said evaporated matrix material to dissolve with said matrix material and to form a crystalline structure on said substrate surface.
- 6. (Amended) A method [according to] of claim 1 [including the step of] wherein the sample material comprises solvent containing [mixing] an analyte material [with] and a matrix material for mass spectroscopy [to form a solution, and filling said interior chamber with said solution].
- 7. (Amended) A method [according to] of claim 1, including the further step of [providing said substrate with said] analyzing the array of sample material disposed thereon [to] with a diagnostic tool [for determining] that determines information [representation] representative of the composition of said sample material.
- 8. (Amended) A method [according to] of claim 7, wherein the [said step of providing said substrate to a] diagnostic tool [includes the step of providing said substrate to a diagnostic tool having] is a mass spectrometer.
- 9. (Amended) A method [according to] of claim 1, wherein [said step of providing a vesicle having an interior chamber includes the step of providing a vesicle having] the vesicle further comprises a piezoelectric element that provides the pressure for [causing fluid to move through] ejecting the nanoliter volume of fluid from the [said] chamber.
- 10. (Amended) A method [according to] of [claim 9] claim 1, wherein said step of moving said vesicle includes the step of rastering said vesicle across said surface of said substrate.
- 11. (Amended) A method [according to] of claim 1, wherein the vesicle part of a said step of providing a vesicle includes the step of providing a vesicle assembly having a plurality of vesicles arranged into a matrix for dispensing fluid to a first plurality of locations [on] onto said substrate surface.

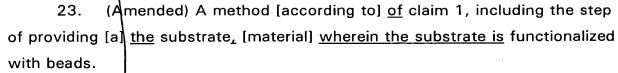


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- 12. (Amended) A method [according to] of claim 11, wherein said step of moving said vesicle [array] includes the step of determining an offset signal representative of a distance for moving [said] the vesicle assembly containing the vesicle to a location [adjacent said] next to the first plurality of locations.
- 13. A method of [according to] of claim 12 wherein said step of moving [said] vesicle [assembly] includes the step of moving said vesicle assembly over said surface of said substrate and dispensing fluid therefrom to form a matrix of locations having fluid ejected thereon.
- 14. (Amended) A method [according to] of claim 1, including the further step of drawing a wash fluid into said chamber of said vesicle to rinse said chamber.
- 15. (Amended) A method [according to] of claim 1, including the further step of contacting said vesicle to a source of fluid material for filling said chamber by capillary action.
- 16. (Amended) A method [according to] of claim 1, including the step of providing [a] the substrate material comprising silicon.
- 17. (Amended) A method [according to] of claim 1, including the step of providing [a] the substrate material comprising a metal material.
- 18. (Amended) A method [according to] of claim 1, including the step of providing [a] the substrate material compromising a plastic material.
- 19. (Amended) A method [according to] of claim 1, including the step of providing [a] the substrate, [material] complising a membrane.
- 20. (Amended) A method [according to of claim 1, including the step of providing [a] the substrate, [material] comprising a polymeric material.
- 21. (Amended) A method [according to] of claim 1, including the step of providing [a] the substrate, [material] comprising metal-grafted polymers.
- 22. (Amended) A method [according to] of claim 1, including the step of providing the substrate, wherein the substrate is a chemically functionalized substrate material.



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- 24. (Amended) A method [according to] of claim 1, including the step of providing [a] the substrate, wherein the substrate is [material] functionalized with a dendritic material.
- 25. (Amended) A method for analyzing a material, comprising: [the steps of]

providing a vesicle [suitable for carrying] <u>comprising</u> a fluid [having said] <u>a</u> <u>containing the material in a solvent[ therein,];</u>

without contacting the surface with the vesicle, disposing said vesicle adjacent to a first location of a surface of [a] the substrate;

[controlling said providing mechanical pressure on the fluid, delivering vesicle to deliver] delivering a defined and controlled nanoliter volume of the fluid [to provide a defined and controlled volume of said fluid] at [said] the first location of said surface of the substrate[,];

moving said vesicle to a second position [adjacent a second] next to the <u>first</u> location on said surface of the substrate to dispense a defined and controlled volume of said material along an array of locations on said substrate surface to form an array of the material[,]; and

performing mass spectrometry analysis for said material at each location of said array.

- 26. (Amended) A method [according to] of claim 25, wherein said step of providing a vesicle, includes the step of mixing a matrix material and an analyte material to form said fluid containing the material.
- 27. (Amended) A method [according to] of claim 25, including the steps of providing a vesicle having an interior chamber suitable for holding [a] the fluid[, and filling said chamber with a matrix material and dispensing said

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matrix material to said array of locations] wherein the material comprises a matrix material for mass spectroscopy.

- 28. (Amended) A method [according to] of claim 25 wherein said step of performing mass spectrometry includes the step of performing matrix assisted laser desorption ionization mass spectrometry.
- 29. (Amended) A method [according to] of claim 25 wherein said step of performing mass spectrometry includes the step of performing a time of flight mass spectrometry analysis.
- 30. (Amended) A method [according to] of claim 25 wherein said step of performing mass spectrometry includes the step of performing a fourier transform mass spectrometry analysis.
- 31. (Amended) [Apparatus] <u>A system</u> for forming an array of a sample material on a surface of a substrate, comprising:
- a vesicle having a distal end suitable for carrying a <u>nanoliter of</u> fluid thereon,];
  - a movable atm having a distal portion mounted to move said vesicle;
- a controller for moving said arm to dispose said vesicle adjacent [at] to a first location on said surface of the substrate and for controlling said vesicle to provide a nanoliter volume of the fluid at said first location of said surface of the substrate; and
- a diagnostic tool for analyzing said material deposited on said surface of said substrate [to generate] by generating a composition signal representative of the chemical composition of said material.
- 32. (Amended) [Apparatus] A system [according to] of claim 31 wherein said vesicle comprises a solid shaft of material.
- 33. (Amended) [Apparatus] A system [according to] of claim 31 wherein said vesicle comprises an interior chamber suitable for carrying a fluid material.

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- 34. (Amended) (Amended) [Apparatus] A system [according to] of claim 31 wherein said vesicle comprises a chamber and a transducer element for ejecting fluid from said chamber.
- 35. (Amended) [Apparatus] A system [according to] of claim 31 wherein said diagnostic tool includes a mass spectrometer.
- 36. (Amended) A substrate having a surface [carrying] comprising an array of sample material selected from matrix material for mass spectrometric analysis or a mixture of the matrix material and analyte deposited at discrete locations thereon wherein the matrix material at each location forms a crystalline structure and comprises an amount that results from deposition of a nanoliter volume containing the material on the surface[ and formed according to a process comprising the steps of providing a vesicle suitable for transferring a fluid containing a matrix material, disposing said vesicle adjacent a first location on said surface of the substrate, controlling said vesicle to deliver a volume of the fluid to said first location of said surface of the substrate and moving said vesicle to a set of positions adjacent said surface of the substrate and delivering fluid at each location of said set, if only matrix or sample is deposited, repeating steps (c) and (d) with matrix material or sample material to provide both matrix material and sample material at each location of the surface of the substrate to form an array of matrix material.
- 37. (Amended) A substrate [according to] of claim 36 having wells disposed on said surface, wherein the sample material is deposited in the wells.
- 38. (Amended) A substrate [according to] of claim 37, wherein said surface is pitted.
- 39. (Amended) A substrate [according to] of claim 37, wherein said wells have a rough interior surface.

#### **REMARKS**

A check for the fees for a three month extension of time and excess claims accompanies this response. If no check is provided or if the check is in